UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/679,201	10/03/2003	Charles A. Dinarello	057878-11	9665

7590 02/14/2007

David S. Resnick, Esq.
NIXON PEABODY LLP
100 Summer Street
Boston, MA 02110

EXAMINER	
WOODWARD, CHERIE MICHELLE	
ART UNIT	**PAPER NUMBER**
1647	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/14/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/679,201	DINARELLO ET AL.	
	Examiner	Art Unit	
	Cherie M. Woodward	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-7,10,41 and 42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-7,10,41 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date *5/31/2006, 7/17/2006*.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

1. Applicant's Amendments, filed 22 November 2006, are acknowledged. Claims 1, 5-7, 10, 41, and 42 are pending. Claims 2-4, 8-9, and 11-40 have been cancelled by Applicants. New claims 41 and 42 have been added. Claims 1, 5-7, 10, 41, and 42 are under examination. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

2. The information disclosure statement (IDS) submitted on 31 May 2006 and 17 July 2006 have been considered by the examiner. Signed copies are attached. It is noted that the Bufler et al., reference cited in the 31 May 2006 IDS submission is missing the date of publication. The date of publication for the Bufler et al., reference is 15 October 2002.

Objections to the Specification Withdrawn

3. The objection to the specification for the use of the trademarks is withdrawn in light of Applicant's amendments.

Claim Objections/Rejections Withdrawn

4. The rejections of claims 2-4 and 11 are moot in light of Applicant's cancellation of the claims. However, new rejections are presented below that are necessitated by Amendment due to Applicant's incorporation of rejected subject matter from claims 2-4 being incorporated into claim 1.

5. The rejection of claims 1, 5-7 and 10 under 35 U.S.C. 102(b) as being anticipated by Kumar et al., WO 2001/40247 A1 (international publication date 7 June 2001, priority to 1 December 1999), is withdrawn in light of Applicant's amendments.

6. The rejection of claims 1, 5-7 and 10 under 35 U.S.C. 102(e) as being anticipated by McDonnell et al., US Patent 6,342,371 B1 (29 January 2002, priority date 16 April 1999), is withdrawn in light of Applicant's amendments.

7. The rejection of claims 1, 5-7 and 10 under 35 U.S.C. 103(a) as being unpatentable over McDonnell et al., US Patent 6,342,371 B1 (29 January 2002, priority date 16 April 1999) and WO

2001/40247 A1 (international publication date 7 June 2001, priority to 1 December 1999; cited by Applicants in IDS of 9 August 2004), in view of Pan et al., (Cytokine 7 January 2001 13(1):1-7; cited by Applicants in IDS of 9 August 2004), in further view of Kumar et al., (Cytokine 21 April 2002 18(2):61-71; cited by Applicants in IDS of 9 August 2004), is withdrawn in light of Applicant's amendments.

Claim Objections/Rejections Maintained

Claim Rejections - 35 USC § 112, First Paragraph

Scope of Enablement

8. The rejection of Claims 1, 5-7, and 10 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of using IL-1F7b, IL-18R, and IL-18BP, in a method for treating rheumatoid arthritis, ulcerative colitis, or Crohn's disease, does not reasonably provide enablement for the method of using other IL-1 family members as cytokine-1 or cytokine-2 receptor proteins, nor other cytokine ligands or receptors in the treatment of a disease, other than rheumatoid arthritis, ulcerative colitis, or Crohn's disease, that is caused or enhanced by induction of a cytokine-2 receptor, is maintained for the reasons of record and for the reason set forth herein.

The claims recite a method of treating or inhibiting a disease that is caused or enhanced by induction of a cytokine-2 receptor in a patient, the cytokine-2 being a member of the IL-1 family, the method comprising administration of an effective amount of a cytokine-1 to bind to the cytokine-2 receptor wherein the cytokine-1 is IL-1F7b and wherein the IL-1F7b is administered together with IL-18BP or mutein, fused protein, functional derivative, or fragment thereof; wherein the cytokine-2 receptor is IL-18R; wherein the disease is an inflammatory disease; wherein the cytokine-1 is administered systemically, subcutaneously, or intramuscularly.

Applicant argues that the amended claims refer to the use of IL-1F7b together with IL-18BP or its functional equivalent(s) that can together bind to a cytokine-2 receptor. Applicant also argues that the Examiner's rejection is not relevant as it relates to whether all diseases that are currently caused by this mechanism are unknown. Applicant argues that the specification describes that the function of IL-18BP variants is their capacity to bind IL-1F7b at paragraph 87. Applicant states that routine experimentation could be used to test IL-18BP variants for this function in order to determine which variants are within the scope of the claims. Applicant also argues that the term inhibition does not read on prevention because the term inhibition refers to inhibiting a condition that already exists as a biochemical manifestation as defined in the claims, which is an activity of a cytokine to which IL-1F7b is capable of binding.

Applicants argue that the method of inhibiting a disease refers to a condition that is clearly defined by the claims. Applicant's arguments and amendments have been fully considered, but they are not persuasive.

Claim 1, as amended, recites a method of treating or inhibiting a disease that is caused by or enhanced by the induction of a cytokine-2 receptor, the cytokine-2 being a member of the IL-1 family, comprising administration of an effective amount of IL-1F7b administered together with IL-18BP or mutein, fused protein, functional derivative or fragment thereof. The disclosure, as originally filed, does not indicate a sufficient number of representative diseases to encompass the genera of diseases that are or may be caused by or enhanced by the induction of an IL-1 receptor. The skilled artisan cannot envision the treatment or inhibition of a disease without knowing which disease is to be treated or inhibited. Similarly, the skilled artisan cannot envision a sufficient number of diseases which comprise the upregulation of an IL-1R, such that the disease could be treated by the claimed method. To suggest that treating any disease involving any IL-1 receptor (through direct causation or enhanced induction), without more, would be entirely unpredictable, and is tantamount to suggesting that every disease involving an enhanced IL-1R response would fall within the scope of the claim. If Applicant's arguments are carried a step farther, the claimed method would, for example, be used treat a common cold or any infection that induced a pro-inflammatory response of any kind. Applicant simply does not have support in the disclosure for the scope or the breadth of the claim, as written.

Additionally, claim 1, as amended, recites that the non-specific, generic disease is to be caused by or enhanced by a member of the IL-1R family. The IL-1R family is comprised of nine distinct IL-1 receptors (see, for exemplary purposes only, Thomson et al., Eds. The Cytokine Handbook, Volume 2, Fourth Edition, Academic Press, San Diego, CA. 2003, at pp. 653-656, especially at p. 653, Table 27.3). The instant disclosure does not teach or provide any guidance as to whether an administered combination of IL-1F7b and IL-18BP or mutein, fused protein, functional derivative, or fragment thereof, will bind to, inhibit, or otherwise antagonize any specific members of the IL-1R family other than IL-18R. Whether the claimed combination will be effective against the other nine primary members of the IL-1R family in any given generic disease, is entirely unpredictable. Thomson et al., Eds., (*supra*) note that IL-17Fb was demonstrated to bind to the IL-18R in precipitation experiments using IL-18Rα-Fc fusion proteins, but that IL-1F7b had no effect on the IFNγ-inducing activity of IL-18 (p. 740, column 2, last paragraph; and p. 741, Table 30.3) (see also, instant specification p. 4 to p. 5, paragraph 12). The assertion that all cytokine-2 receptors of the IL-1R family have biological activities similar to known IL-18R cannot be accepted in the absence of supporting evidence, because the relevant literature reports that IL-1F7b binds to IL-18R in *in vitro* experiments and the instant disclosure fails to provide guidance beyond what is known in the art, relative to IL-1F7b and/or IL-18BP binding partners. Enablement must be provided by the specification unless it is well known in the art. In re Buchner 18 USPQ 2d 1331 (Fed. Cir. 1991). Again, Applicant simply does not have support in the disclosure for the scope or the breadth of the claim, as written.

Claim 1, as amended, embraces a broad class of structural fragments and functional derivatives that are not taught in the specification. As such, the skilled artisan is not provided with sufficient guidance as to how to make or use the claimed generic IL-18BP muteins, fused proteins, functional derivatives, or fragments thereof. There is no guidance or teaching in the specification as to the structure of any muteins, fused proteins, functional derivatives, or fragments thereof. Similarly, there is no teaching related to whether these muteins, fused proteins, functional derivatives, or fragments thereof should retain IL-18BP function. Although the term "functional derivatives" is defined in the specification (p. 29, paragraph 0099), but no guidance is provided as to which function(s) are referred to. Retention of IL-18BP function in muteins, fusion proteins, functional derivatives, or fragments thereof cannot be assumed by one of skill in the art, absent such a limitation in the claims and support for the limitation in the specification. Further, the disclosure fails to provide sufficient guidance on how to make the claimed muteins, fused proteins, functional derivatives, or fragments thereof such that it can be determined how to use the claimed generic polypeptide components in the claimed method of treatment. Instead, the specification provides an invitation for further experimentation. Such an invitation would require much more than routine experimentation in order to determine the structure and function of the claimed muteins, fusion proteins, functional derivatives, or fragments thereof, and to determine whether the claimed muteins, fusion proteins, functional derivatives, or fragments thereof would actually work in the claimed method. For example, the breadth of claimed "functional derivatives" includes naturally occurring viral proteins, such as the ectromelia poxvirus p13 protein (see paragraph 10, p. 3 of the specification).

Claim 5 has support in the specification, insofar as the cytokine-2 receptor is IL-18R. However, claim 5 remains deficient for the scope of treating or inhibiting non-specific generic diseases using IL-18BP muteins, fusion proteins, functional derivatives, or fragments thereof, as stated above.

Claim 6 remains deficient as it recites generic cytokine-2 receptors, and the specification lacks support for use of the claimed method in all IL-1R family members and for the scope of treating or inhibiting non-specific generic diseases using IL-18BP muteins, fusion proteins, functional derivatives, or fragments thereof, as stated above.

Claim 7 remains deficient because the specification lacks support for use of the claimed method in all IL-1R family members and for the scope of treating or inhibiting non-specific generic inflammatory diseases using IL-18BP muteins, fusion proteins, functional derivatives, or fragments thereof, as stated above.

Claim 10 remains deficient because the specification lacks support for all of the reasons stated above.

The teachings of the specification do not enable a person of ordinary kill in the art to make or use the claimed method as written. "Patent protection is granted only in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable." Genentech Inc. v. Novo Nordisk A/S, 108 F.3d at 1366, 42 USPQ2d at 1005 (Fed. Cir.), cert. denied, 118 S. Ct. 397 (1997), ("Tossing out the mere germ of an idea does not constitute an enabling disclosure").

Due to the large quantity of experimentation necessary to determine which disease is caused by or enhanced by the induction of an IL-1R family member, such that it can be determined how to use the claimed polypeptides in the claimed method of treatment, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, and the breadth of the claims which fail to recite particular diseases, cytokines, or receptors and also embrace a broad class of structural fragments and functional derivatives, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 112, First Paragraph
Written Description

9. The rejection of claims 1, 5-7, and 10 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement as it relates to diseases that are caused by or enhanced by IL-1R family members, functional derivatives of IL-18BP, and cytokine-2 receptors or cytokine-1 polypeptides, is maintained for the reasons of record and the reasons stated herein.

The claims recite a method of treating or inhibiting a disease that is caused or enhanced by induction of a cytokine-2 receptor in a patient, the cytokine-2 being a member of the IL-1 family, the method comprising administration of an effective amount of a cytokine-1 to bind to the cytokine-2 receptor wherein the cytokine-1 is IL-1F7b and wherein the IL-1F7b is administered together with IL-18BP or mutein, fused protein, functional derivative, or fragment thereof; wherein the cytokine-2 receptor is IL-18R; wherein the disease is an inflammatory disease; wherein the cytokine-1 is administered systemically, subcutaneously, or intramuscularly.

Applicant argues that the amended claims comply with the written description requirement. Applicant also argues that the structure of IL-18BP is well known and that the functional requirements for the claims are described in, for example, paragraph 87 and Example 3. Applicant's arguments have been fully considered, but they are not persuasive.

It is unclear where Applicant finds support for the argument that the functional requirements for IL-18BP muteins, fusion proteins, functional derivatives, or fragments thereof, are adequately described in paragraph 87. Paragraph 87 of the specification (see p. 23) describes cross-linking experiments in which IL-1F7b binds to IL-18BP and by analogy to IL-18. Paragraph 87 also states that "[s]ince IL-1F7b in complex with IL-18BP is not able to bind to IL-18Rα, inhibition of IL-18 activity is probably caused by binding of such complex to the signaling IL-18Rβ chain. The β-chain therefore, may be recruited to the complex, depriving the β-chain to form a functional receptor complex with IL-18Rα and IL-18." Similarly, it is unclear where Applicant finds support for the argument that the functional requirements for IL-18BP muteins, fusion proteins, functional derivatives, or fragments thereof, are adequately described in Example 3. Example 3, found on pages 36-37 of the specification (paragraphs 127-130), states that IL-1F7b shares two amino acids in common with IL-18 and "based on the sequence similarity of IL-1F7b and IL-18BP, the possibility that IL-1F7b binds to IL-18BP was investigated." It is unclear whether Applicant is arguing that Example 3 describes any polypeptide of any length, comprising any amino acid in any position, so long as it comprises E42 and K89. It is also unclear whether Applicant is suggesting that an unknown generic structure comprising E42 and K89 will function as an IL-18BP mutein, fusion protein, functional derivative, or fragment thereof. The description of two amino acids, even if critical for functional purposes, without more, is insufficient to provide adequate written description for a class of muteins, fusion proteins, functional derivatives, or fragments thereof. The structure and function of polypeptides are important to the written description requirement. It is through the structure/function description that Applicant shows that they were in possession of the claimed subject matter at the time of the invention.

10. The rejection of claims 1 and 6 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained for the reasons of record and the reasons set forth herein. Claim 6 recites the method of claim 1, wherein the cytokine-1 binds to the signaling chain of the cytokine-2 receptor. The disclosure fails to adequately describe a "signaling chain."

Applicant argues that page 4, paragraph 12 of the specification describes an example of signaling chains. Applicants state that "the activity of the cytokines in the cytokine-1 family is mediated via a receptor complex consisting of the ligand-binding chain and a signaling chain. Upon binding of a ligand to the ligand-binding chain and the formation of the heterocomplex with the signaling chain, the cytokine induces activation of its pathway." Applicant also argues that while this is exemplified using IL-18, similar mechanisms are known in other IL-1 family cytokines. Applicant's argument has been fully considered, but it is not persuasive.

In essence, it appears that Applicant is arguing that because a signaling chain for IL-18 is described in the specification, all other IL-1 family cytokine signaling chains are described by analogy. This line of reasoning is unsupported by any description in the disclosure and is simply not supported in the art.

As explained *supra*, amended claim 1, upon which claim 6 depends, recites the method wherein the cytokine-2 receptor is a member of the IL-1R family. The IL-1R family is comprised of nine distinct IL-1 receptors (see, for exemplary purposes only, Thomson et al., Ed., *supra*, at pp. 653-656, especially at p. 653, Table 27.3). The instant disclosure does not describe whether an administered combination of IL-1F7b and IL-18BP or mutein, fused protein, functional derivative, or fragment thereof, will bind to, inhibit, antagonize, or other wise affect the signaling chain of any of the members of the IL-1R family other than IL-18R. The signaling chains of other members of the IL-1R family are not described in the specification, such that one of skill in the art would understand that IL-1F7b binds to the signaling chains of other IL-1R family members. Applicant has described that IL-1F7b binds to IL-18BP (see Example 3) and paragraph 87 of the specification (see p. 23). Paragraph 87 states that "[s]ince IL-1F7b in complex with IL-18BP is not able to bind to IL-18Rα, inhibition of IL-18 activity is probably caused by binding of such complex to the signaling IL-18Rβ chain. The β-chain therefore, may be recruited to the complex, depriving the β-chain to form a functional receptor complex with IL-18Rα and IL-18." However, there is no description of whether IL-1F7b binds to other members of the IL-1R family signaling chains such that it could be determined whether other members of the IL-1R family share the same signaling chain as IL-18BP or whether IL-1F7b binds to and/or affects the signaling chains of any other members of the IL-1R family. Only the IL-18Rβ signaling chain is described in the specification.

Claim Rejections - 35 USC § 112, Second Paragraph

11. The rejection of claims 1 and 6 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the

invention, is maintained for the reasons of record and the reasons set forth herein. Claim recites the method of claim 1, wherein the cytokine-1 binds to the signaling chain of the cytokine-2 receptor. The disclosure fails to teach what a "signaling chain" is or where it could be found on any given cytokine-2 receptor. The metes and bounds of a "signaling chain" are not disclosed.

Applicant argues that the rejection under 35 USC 112, second paragraph regarding the metes and bounds of the term "signaling chain" should be withdrawn by reference to Applicant's argument presented in response to the Written Description rejection (*supra*) regarding signaling chains. As such, Applicant argues that page 4, paragraph 12 of the specification describes an example of signaling chains. Applicants state that "the activity of the cytokines in the cytokine-1 family is mediated via a receptor complex consisting of the ligand-binding chain and a signaling chain. Upon binding of a ligand to the ligand-binding chain and the formation of the heterocomplex with the signaling chain, the cytokine induces activation of its pathway." Applicant also argues that while this is exemplified using IL-18, similar mechanisms are known in other IL-1 family cytokines. Applicant's argument has been fully considered, but it is not persuasive.

Applicant has failed to disclose the metes and bounds of the term "signaling chain" as applied to the IL-1R family of cytokine receptors. Amended claim 1, upon which claim 6 depends, recites the method wherein the cytokine-2 receptor is a member of the IL-1R family. The IL-1R family is comprised of nine distinct IL-1 receptors (see, for exemplary purposes only, Thomson et al., Ed., *supra*, at pp. 653-656, especially at p. 653, Table 27.3). The signaling chains of other members of the IL-1R family are not mentioned in the specification, such that one of skill in the art would understand that IL-1F7b binds to the signaling chains of other IL-1R family members. Applicant has described that IL-1F7b binds to IL-18BP (see Example 3) and paragraph 87 of the specification (see p. 23). Paragraph 87 states that "[s]ince IL-1F7b in complex with IL-18BP is not able to bind to IL-18Rα, inhibition of IL-18 activity is probably caused by binding of such complex to the signaling IL-18Rβ chain. The β-chain therefore, may be recruited to the complex, depriving the β-chain to form a functional receptor complex with IL-18Rα and IL-18." However, there is no information as to whether IL-1F7b binds to other members of the IL-1R family signaling chains such that it could be determined whether other members of the IL-1R family share the same signaling chain as IL-18BP or whether IL-1F7b binds to and/or affects the signaling chains of any other members of the IL-1R family. Only the IL-18Rβ signaling chain is discussed in the specification.

New Claim Objections/Rejections – Necessitated by Amendment
Claim Rejections - 35 USC § 112, First Paragraph
Scope of Enablement

12. Claims 41 and 42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of coadministering IL-1F7b and IL-18BP, in a method for treating IL-18R induced rheumatoid arthritis, ulcerative colitis, or Crohn's disease, does not reasonably provide enablement for the method of coadministering IL-1F7b and IL-18BP, in a method for treating IL-18R induced generic inflammatory disease.

The claims recite a method of treating an inflammatory disease that is caused or enhanced by induction of a cytokine-2 receptor in a patient in need thereof, the cytokine-2 being IL-18, the method comprising administration of an effective amount of a cytokine-1 to bind to the cytokine-2 receptor wherein the cytokine-1 is IL-1F7b and wherein the IL-1F7b is administered together with IL-18BP; wherein the disease is arthritis, ulcerative colitis, or Crohn's disease.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability, 5) existence of working samples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The invention is directed to a method of treating an inflammatory disease that is caused by induction of the IL-18R, comprising administering an effective amount of IL-1F7b in combination with IL-18BP to a patient in need thereof. The state of the prior art is such that methods of treating chronic and acute inflammation with IL-1F7b (also known as IL-1H4, see, i.e. specification at p. 23, paragraph 85) is known in the art (see Kumar et al., WO 2001/40247, cited in the Office Action of 24 May 2006). However, the art does not teach administration of IL-1F7b in combination with IL-18BP. The art also teaches IL-18 dysregulation in rheumatoid arthritis (Gracie et al., J Clin Invest. 1999 Nov;104(10):1393-401; cited in Applicant's IDS of 8/9/2004), in Crohn's disease and ulcerative colitis (see Pizarro et al., J Immunol. 1999 Jun 1;162(11):6829-35; cited in Applicant's IDS of 8/9/2004; and Monteleone et al., J Immunol. 1999 Jul 1;163(1):143-7; also cited in Applicant's IDS of 8/9/2004).

However, claim 41 is drawn to treatment of any inflammatory disorder. Inflammatory disorders can range from infections of any kind to allergic reactions to chronic autoimmune disease to arteriosclerosis – basically any disorder with an inflammatory component. The scope of Applicant's claims are not supported by the art or the instant specification. The instant specification notes that IL-18 dysregulation has been found in rheumatoid arthritis (paragraph 31, p. 11), Crohn's disease, and ulcerative colitis (paragraphs 51-52, pages 15-16). However, Applicant also lists other disorders for which there has been no definitive IL-18 dysregulatory disease connection. For example, the specification states that "[I]t has been suggested that IL-18 is involved in the progression of pathogenicity in chronic inflammatory diseases..." (paragraph 13, p. 5). "Liver damage or injury may have diverse causes" (paragraph 14, p. 5). As such, determining the presence of IL-18 dysregulation in any given inflammatory disease, without more, is entirely unpredictable.

Claim 42 is dependent on claim 41 and is drawn to any type of arthritis, ulcerative colitis, and Crohn's disease. There are approximately 122 different types of arthritis (see, for exemplary purposes only, the Arthritis Foundation, Disease Center, 2/7/2007, attached). Applicant has only provided guidance showing that IL-18 is dysregulated in rheumatoid arthritis, one specific species among more than 100 different types of arthritis. The catch-all term "arthritis" describes a genera of multifaceted pathologies that may be mechanical, inflammatory, infectious, acute, chronic, genetic, or some combination thereof, in nature. The term "arthritis" is not a defined set of disorders with similar symptoms or disease etiologies, such that one could define the whole genera with merely one or two exemplary species. Applicant has failed provided guidance such that one of skill in the art would be able to determine which species of arthritis exhibits IL-18 dysregulation without undue experimentation. Without sufficient guidance to determine which type of arthritis exhibits IL-18 dysregulation, using the claimed method to treat patients with any of the disorders within the genera of "arthritis" would be entirely unpredictable.

The teachings of the specification do not enable a person of ordinary kill in the art to make or use the claimed method, as written. Due to the large quantity of experimentation necessary to determine which inflammatory disease is treatable by the claimed method, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, and the breadth of the claims which fail to recite particular diseases with IL-18 dysregulation other than rheumatoid arthritis, Crohn's disease, and ulcerative colitis, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Conclusion

NO CLAIM IS ALLOWED.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cherie M. Woodward whose telephone number is (571) 272-3329. The examiner can normally be reached on Monday - Thursday 9:00am-7:30pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CMW
AU 1647

Marianne P. Allen

MARIANNE P. ALLEN
PRIMARY EXAMINER 2/8/07

AU 1647